Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about the work.

The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission: Supplementary material

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Supplementary methods

Contact definition

Contacts were defined as follows in line with national guidelines:[1] a person who has been close to someone who has tested PCR-positive for COVID-19 anytime from 2 days before the person was symptomatic up to 10 days from onset of symptoms. The nature of the contact could include:

- Living in the same household OR
- Face to face contact (within 1 metre for any length of time) or skin to skin contact or someone the case coughed on OR
- Within 1 metre for 1 minute of longer OR
- Within 1-2 metres for more than 15 minutes OR
- Sexual contacts OR
- Travel in the same vehicle or a plane

Contacts named by more than one index patient in a 10-day period were excluded given ambiguity about the infection source if the contact tested positive.

The contact tracing data provided contained a single contact event type (household/accommodation, household visitor, events/activities, or work/education) per case-contact pair, which was determined by the original contact tracer in more specific categories which were then aggregated.

Vaccination status

Index cases and contacts were included where their vaccination status, obtained from National Immunisation Management Service, was known. Matching was performed using NHS numbers, which are unique to each person in the UK. As all vaccination records included an NHS number, absence of a matched record was classified as unvaccinated, accepting a small amount of misclassification from individuals vaccinated in other countries or in trials. Only individuals vaccinated with Pfizer-BioNTech BNT162b2 and AstraZeneca ChAdOx1 were included, as numbers receiving other vaccines were too few to analyse.

Classification of variants

Contacts of index cases tested between 01-January-2021 and 31-July-2021 were included as follows. Index cases with S-gene target failure (SGTF), used as a proxy for the Alpha (B.1.1.7) variant, were included up to 06-June-2021. During this period 5-95% of sequenced infections were due to Alpha.[2] However following 06-June-2021, the Alpha variant accounted for ≤2% of cases/week[2] (Figure S1), such that there was ambiguity about whether S gene target failure (SGTF) was due to Alpha or stochastic failure to amplify the S gene target at low viral loads with other lineages (predominantly Delta), which occurred in 1% of samples when Delta dominated at the end of July-2021. From the week beginning 10-May-

2021 national spread of Delta meant that >98% of sequenced cases were either due to the Alpha or Delta variants,[2] such that we used detection of S gene on or after 10-May-2021 as a proxy for the Delta variant. Index cases without SGTF prior to 10-May-2021 were excluded, as it was not possible to distinguish which cases had the Delta variant.

Statistical methods details

We used multivariable Poisson regression to investigate how onward transmission, i.e., SARS-CoV-2 PCR-positive tests in contacts, varied with index case vaccination status, contat vaccination status, and other variables. Poisson regression with robust standard errors[3,4] was used in place of logistic regression to improve interpretability of model outputs given a common binary outcome.

We investigated associations between onward transmission and index case vaccination status, using a five-level categorical variable: unvaccinated, partially vaccinated with AstraZeneca ChAdOx1 (first vaccine date to 13 days after second vaccine), partially vaccinated with Pfizer-BioNTech BNT162b2, vaccinated twice with ChAdOx1 (≥14 days after second vaccine) and vaccinated twice with Pfizer-BioNTech BNT162b2. The same five-level categorical formulation was used for contact vaccination status.

We investigated how onward transmission changed with Alpha vs. Delta index cases as a main effect, and whether vaccine-transmission associations varied by variant using pre-specified interaction terms between index case vaccination status and variant and contact vaccination status and variant.

We used natural cubic splines and log transformation to account for non-linear effects of continuous variables following truncation at the 1st and 99th centiles, for splines allowing up to 5 default-placed knots (9 for calendar time to allow greater flexibility) and choosing the best fitting models using the Bayesian information criterion (BIC). Time since second vaccination for cases and contacts was $\log_2$ transformed (on the basis of model fit), truncating time separately for each vaccine. Interactions between all model main effects were included with this improved model fit based on the BIC.

We used robust standard errors with clustering based on index case identifier to account for some index cases being included in the analysis more than once if the index case had multiple contacts not named by any other source.

All analyses were performed in R, version 4.1. The sandwich library's (version 3.0) vcovCL function was used to generate variance-covariance matrices accounting for repeated measurements. Heterogeneity rate ratios and 95% confidence intervals were calculated using interaction terms and contrasts between levels of categorical variables (determined using the glht function from the multicomp library [version 1.4]).

Extent of vaccine-associated reductions in transmission mediated via index case Ct values at diagnosis

We refitted models including index case Ct values to investigate the relationship between Ct values (indicative of viral load[5]) and transmission. We fitted the same final model as obtained for the main analysis, and added a non-linear term spline-based term for Ct value (with up to five default placed knots as above). We tested for interactions between Ct value and all model main effects, retaining a single interaction with variant (Alpha vs. Delta) based on model fit using BIC as above.

As we find that vaccination status can impact index case Ct values, at least for Alpha variant infections, and that Ct values at index case diagnosis are associated with onward transmission, we performed a mediation analysis to assess the proportion of the total effect of index case vaccination on onward transmission that is mediated via changes in index case Ct values. To facilitate a mediation analysis using readily available methods, we fit separate models for the Alpha and Delta variants, and approximate the relationship between Ct value and onward transmission as linear (Figure 4B). Otherwise, the main outcome model remains the same. For the model representing the value of the mediator, Ct value, we use linear regression and the following covariates: index case vaccination status, time since 2nd index case vaccination, index case age (allowing for non-linearity), index case sex, index case symptoms and calendar time (also as a non-linear term). Analyses were performed using the mediate (version 4.5) package in R. Confidence intervals were generated using 1000 simulations and robust standard errors.

Sensitivity analyses – time window between case and contact PCR tests

We undertook two analyses to justify the choice of requiring contacts to be tested within 1-10 days of the index case. In the first we exploit that the likelihood of onward transmission and a PCR-positive result in a contact is approximately linearly related to the PCR Ct value recorded for the index case at diagnosis.[6] It therefore follows that where the index case is the true source, we expect this relationship to be strongest, averaging over all possible intervals from the contact event to testing of the index case. Conversely, if we fail to identify the true index case then this relationship will attenuate towards no effect. We can therefore use this property to estimate what range of time intervals between index case test and contact test that are consistent with transmission, specifically in the direction from the index case to the contact. The initial plausible range of times is determined using prior data on the serial interval between cases in a transmission chain.[7] We fitted univariable logistic regression models of the association between PCR-positive results in contacts and the Ct value in the putative index case. We fitted separate models for case-contact pairs where the contact's PCR test occurred -3, -2, -1, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or 13 days after the index case's PCR test. We fitted separate models for each day for Alpha and Delta variant index case infections. We then report how the odds ratio for a PCR-positive result in the

contact per unit change in index case Ct value varied by time interval between case and contact tests.

In a separate sensitivity analysis we repeated the main analysis restricting to index cases and contacts where the contact was tested between 2 and 7 days following the index case.

Supplementary results

Excluded index cases and contacts

A total of 27,217 contacts were excluded with incomplete data (15.7%): 16,999 contacts had no recorded vaccine status, 11 missing index case Ct values, 9,849 missing a contact event type, 182 index case sex, 5 contact sex, and 171 contact's local area. The remaining 146,243 case-contact pairs had complete data for all study covariates.

Relationship between index case Ct value and onward transmission, by time between index case and contact PCR tests

The most common time interval between index case and contact PCR tests was 0 days, with most other contacts tested in the 7 days following the index case (Figure S5A).

The odds ratio for a PCR-positive test in the contact per unit change in index Ct value varied by the time interval between case and contact PCR tests (Figure S5B). For Alpha variant infections, the odds ratio was greatest for contact PCR tests done 1 to 10 days after the index case. For Delta, the odds ratio was greatest for tests 1 to 6 days after the index case. This suggests that these time intervals are most enriched for index cases that are the true source for the infection in their contact. Whereas, for 'contacts' tested before index cases the odds ratio attenuated to near 1, i.e. no effect, suggestive that the contacts acquired their infection from another source (some may even have been the source of the 'index case's' infection). As relatively few contacts were tested >7 days after the index case, the upper limit set on the time interval between tests is less critical.

Sensitivity analysis restricting to contacts tested 2-7 days after an index case

Findings were similar to the main analysis. A table analogous to Table 1 for the sensitivity analysis is shown as Table S7 and a figure analogous to Figure 1 as Figure S8.
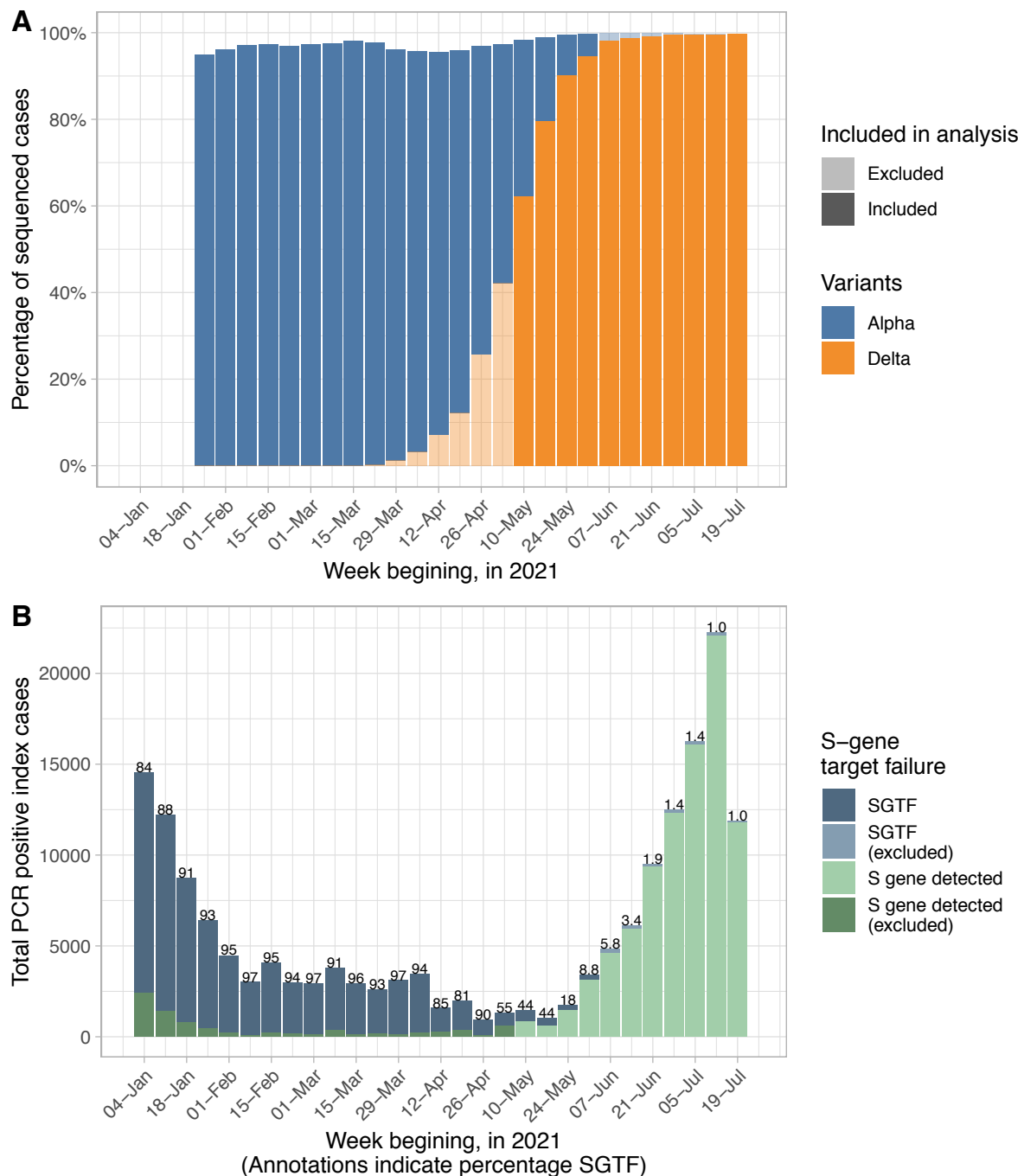
Figure S1. National incidence of Alpha and Delta variants as determined by whole genome sequencing (panel A) and index case incidence according to S-gene target failure (SGTF, panel B). In panel A, weeks for which index cases with presumed Alpha and Delta infections (see Methods) were included in the analysis are shown in the denser shading (sequencing not used to determine variant as not available for all index cases). Based on results of national sequencing data available at
https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-

[variant-of-concern-20201201](). SGTF was seen in 1% of infections in the final two weeks of the study when Delta accounted for nearly all infections. Hence by only classifying index cases Alpha variant on the basis of SGTF in weeks where Alpha prevalence by sequencing exceeded ≥5% we ensured misclassification was minimised. In panel B the percentage of index cases with SGTF is provided above each bar.

Figure S2. Relationship between contact age and variant and probability of a positive PCR test in a contact. All other continuous covariates are set to median values and categorical covariates to reference categories. The error bars indicate 95% confidence intervals.

Figure S3. Relationship between local SARS-CoV-2 incidence and probability of a positive PCR test in a contact. All other continuous covariates are set to median values and categorical covariates to reference categories. The shaded area indicates the 95% confidence interval.
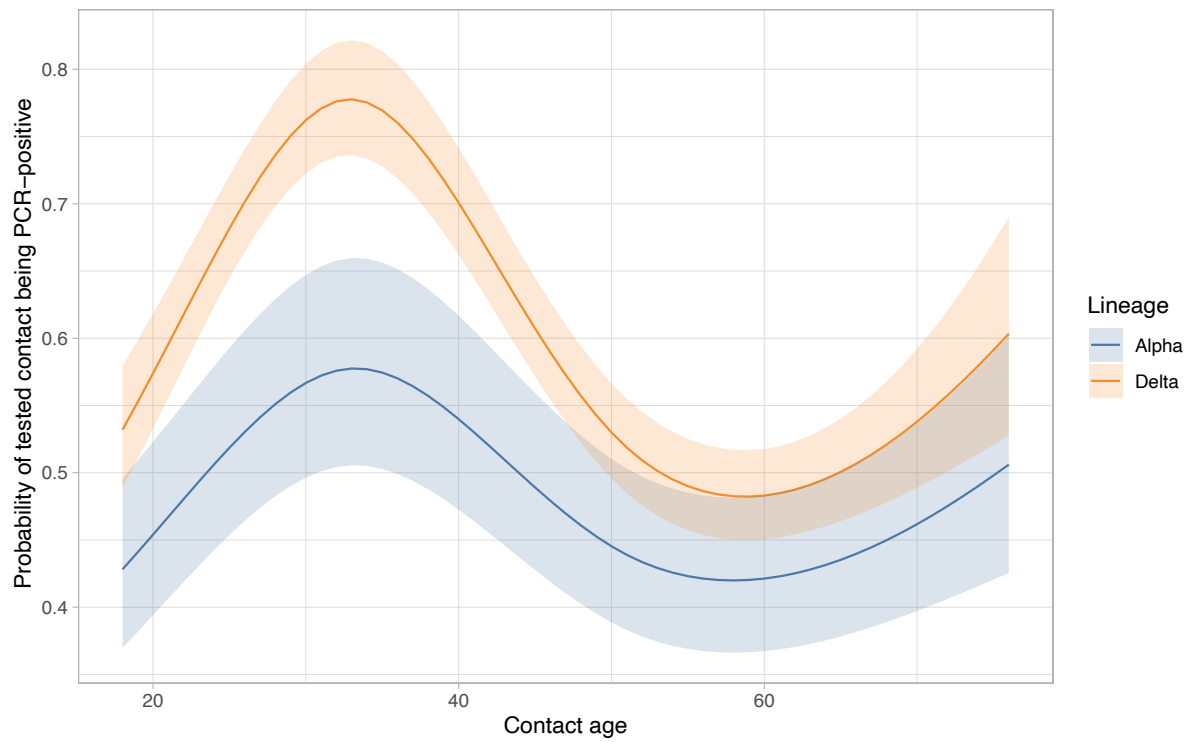
Figure S4. Relationship between study day and probability of a positive PCR test in a contact. All other continuous covariates are set to median values and categorical covariates to reference categories. The shaded area in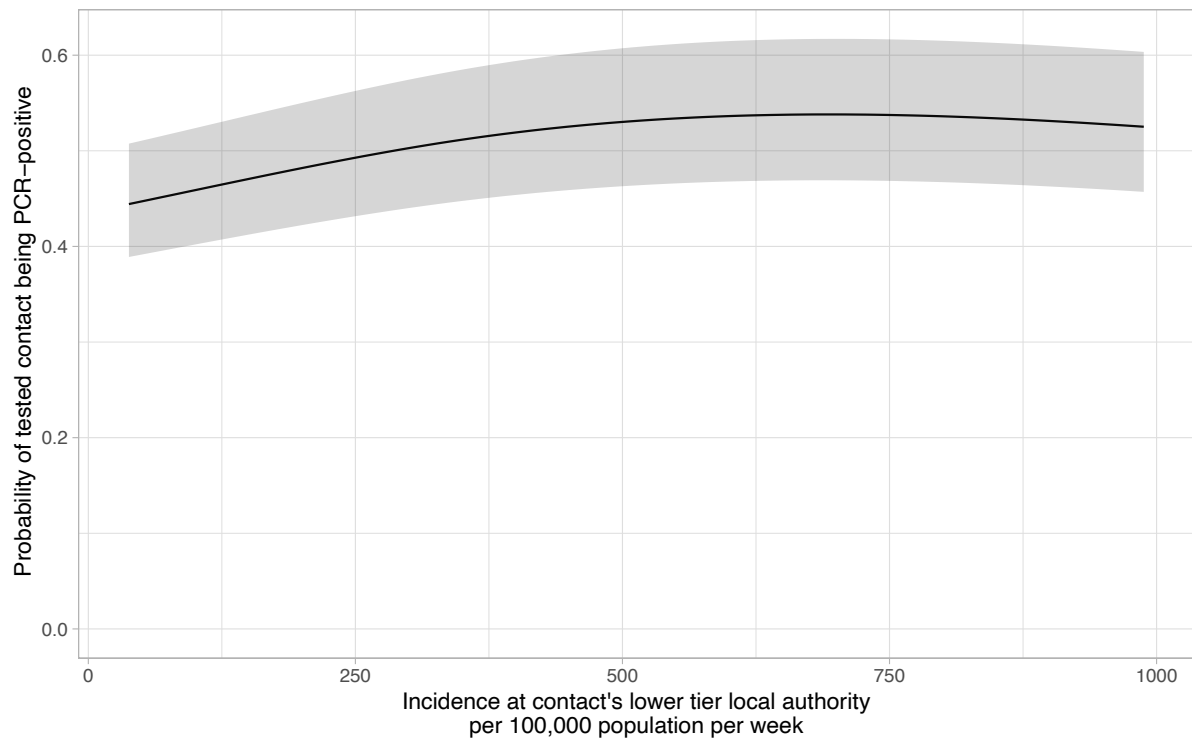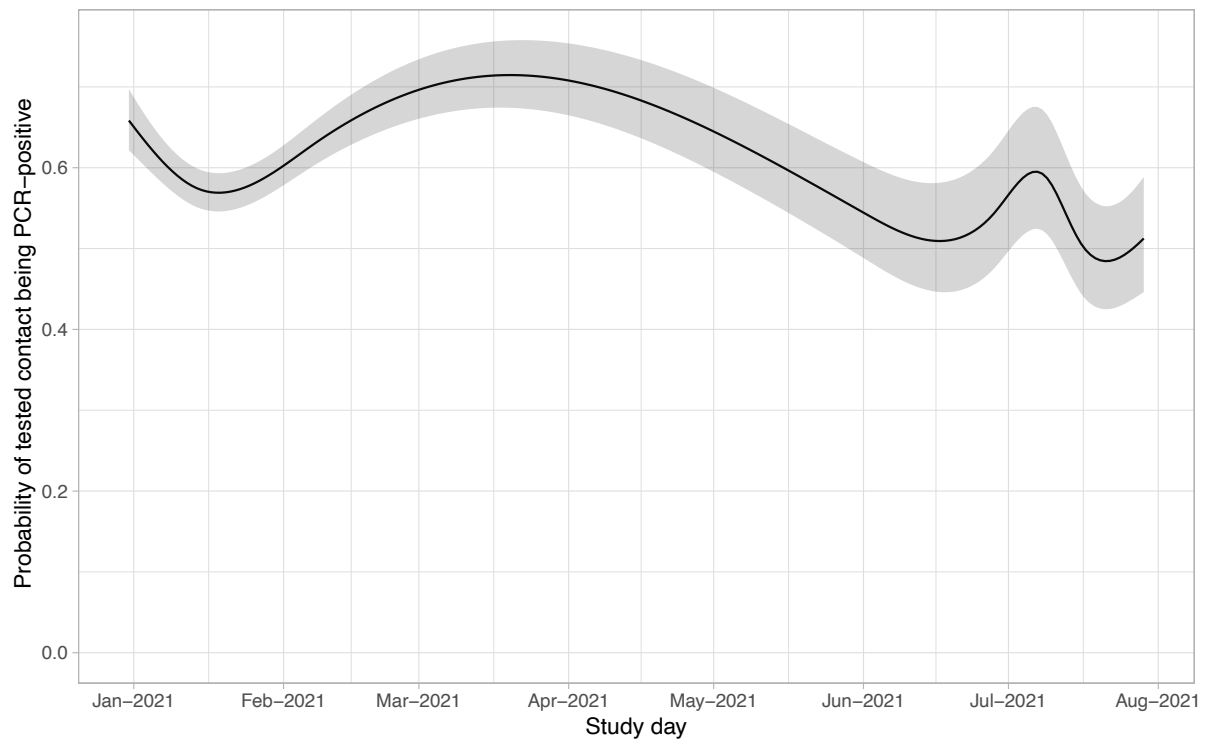dicates the 95% confidence interval. Note "UEFA Euro 2020" European Football Championship held between 11 June and 11 July 2021.

Figure S5. Estimated probability of a positive PCR test in contacts by time since second vaccination in index cases (panel A) and in contacts (panel B), variant, and vaccine type. For panel A estimates are displayed for an unvaccinated contact and a contact vaccinated twice with BNT162b, at 12 weeks post second dose. For panel B estimates are shown for an unvaccinated index case and an index case vaccinated twice with BNT162b, at 12 weeks post second dose. The dashed horizontal lines indicate the probability of a positive-PCR result in an unvaccinated contact of an unvaccinated index case. The shaded area indicates the 95% confidence interval. Adjustment made for covariates, set to reference values: contact event type (set to Household or accommodation); index case factors – age (median), sex (female), and symptom status (symptomatic); contact factors – age (median), sex (female); local deprivation (median), local SARS-CoV-2 incidence (median) and calendar time (median). Note only 26.2% of contacts had a PCR test, as testing was predominantly only performed if symptoms developed. Therefore, overall secondary attack rates are lower than shown here restricting only to contacts undergoing testing.
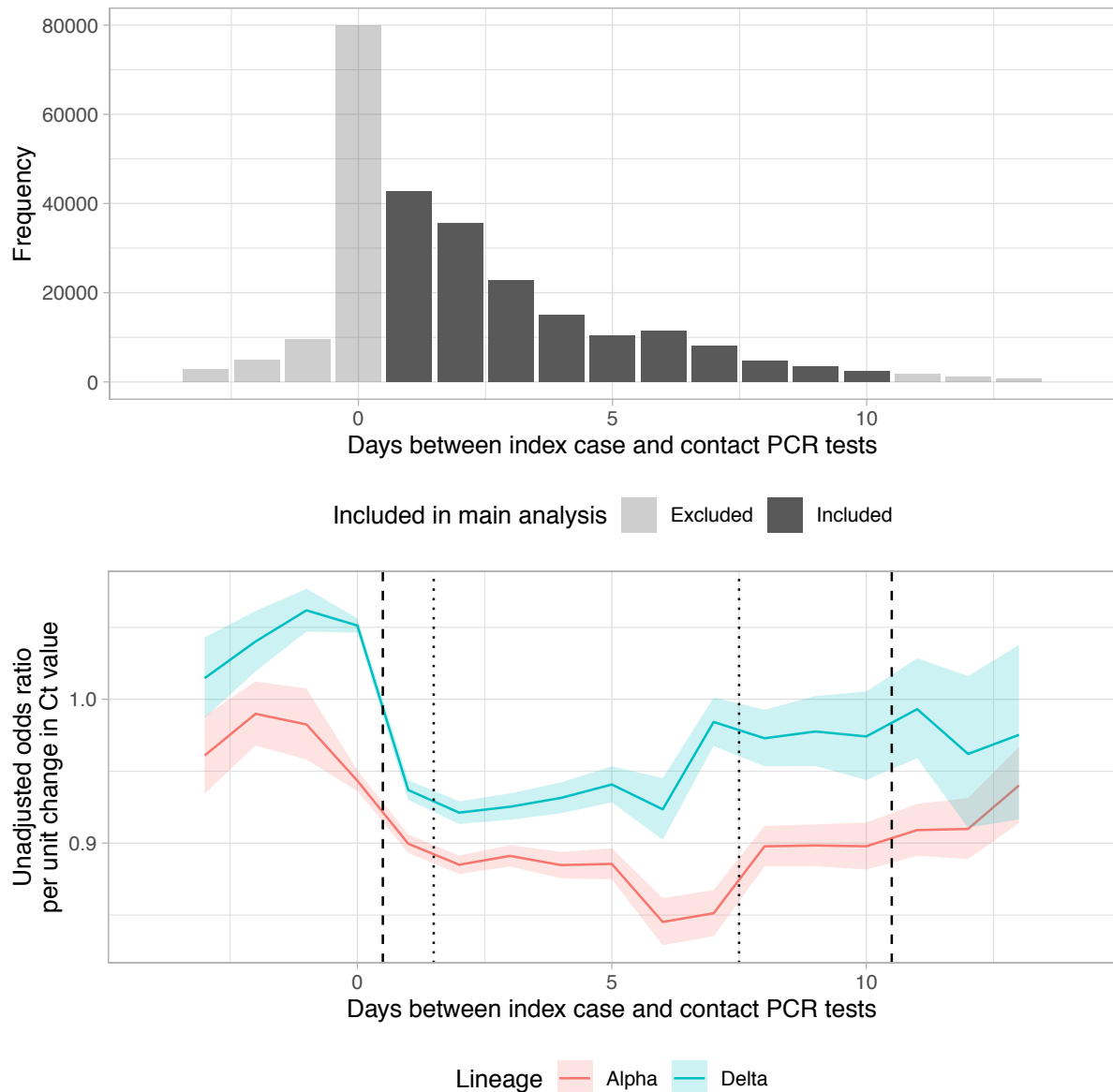
Figure S6. Relationship between index case Ct value and onward transmission, by time between index case and contact PCR tests. Panel A shows the distribution of days between index case and contact PCR tests in case-contact pairs, shaded according to which pairs were included in the main analysis. Panel B shows the univariable odds ratio for a positive-PCR result in a contact for each unit change in index case Ct value, according to days between index case test and contact test and SARS-CoV-2 variant. The dashed vertical lines indicate the cut-offs for inclusion in the main analysis (days 1-10 inclusive) and the dotted vertical lines the cut-offs for inclusion in a separate sensitivity analysis (days 2-7 inclusive).

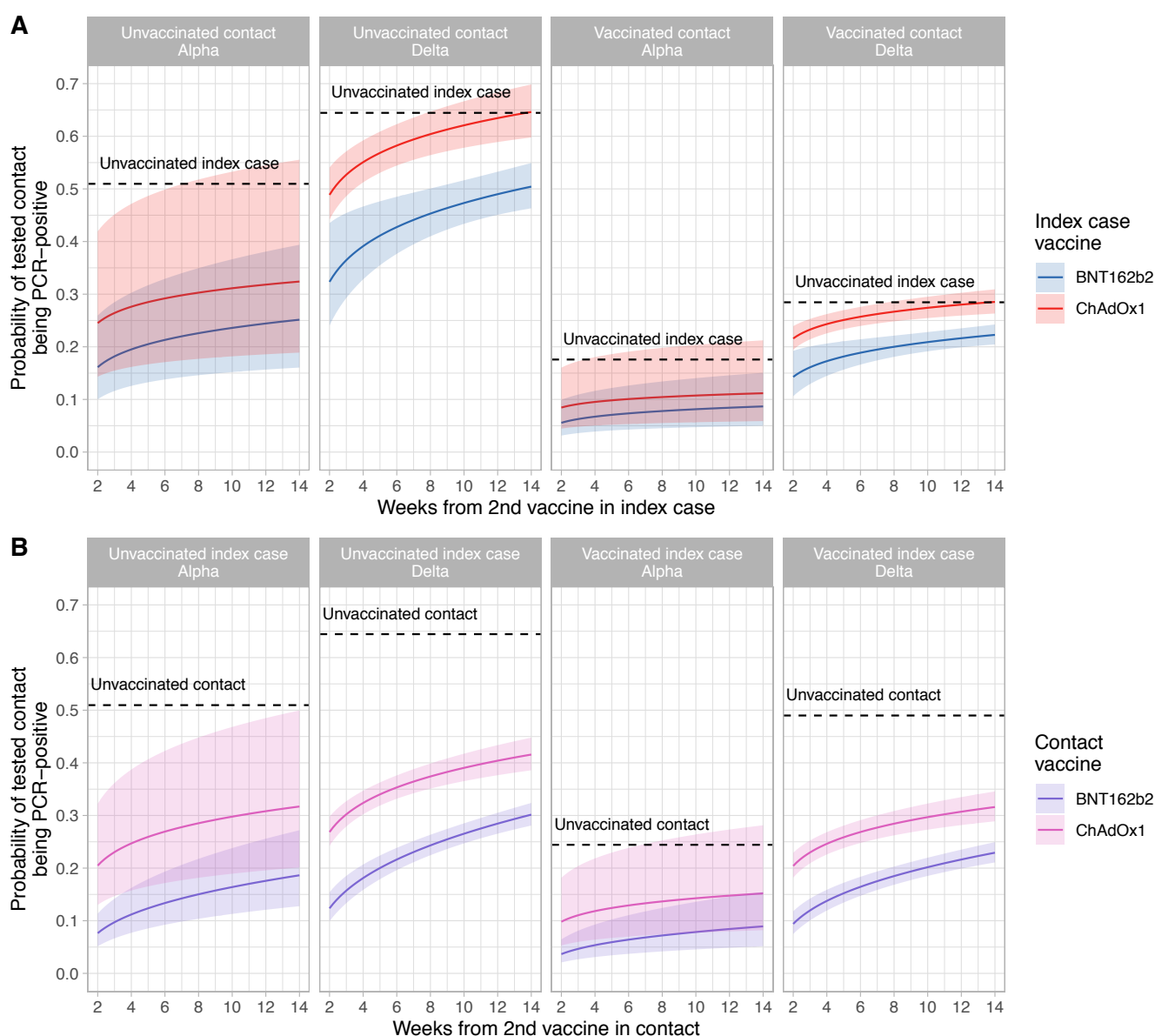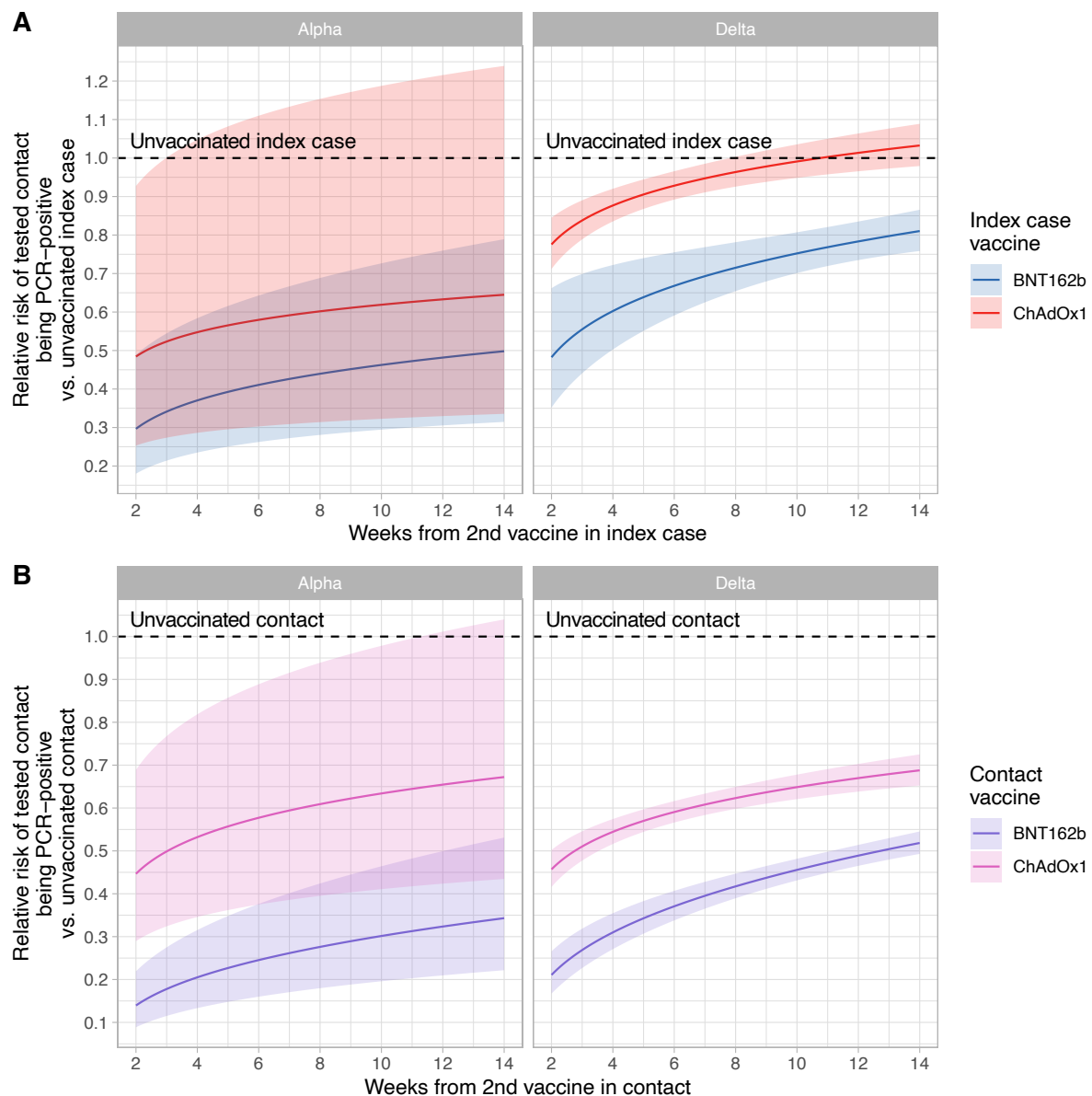**Figure S7. Sensitivity analysis: Rate ratios for positive PCR tests in contacts by time since second vaccination in index cases (panel A) and in contacts (panel B), variant, and vaccine type (restricting to contacts tested 2 to 7 days inclusive after an index case).** Panel A compares the rate of positive PCR results in test contacts, comparing index case vaccination status to an unvaccinated index case. Panel B compares the rate of positive PCR results in test contacts, comparing contact vaccination status to an unvaccinated contact. The shaded area indicates the 95% confidence interval.

Model factors	Description		Notes
Main exposures	Index patient vaccination status		Pre-specified interaction with index patient SARS-CoV-2 variant included
	Index patient SARS-CoV-2 variant		Alpha; Delta
Covariates	Contact event type		
	Index patient factors	Age	
		Sex	
		Symptom status	Symptoms were determined at the point of contact tracing, which followed a positive PCR test in the index case. Therefore, individuals who were symptomatic or pre-symptomatic at the contact event are classed as symptomatic. Those who had no symptoms up to the point of contact tracing are recorded as asymptomatic.
	Contact factors	Age	
		Sex	
		Vaccination status	Pre-specified interaction with index patient SARS-CoV-2 variant included
	Local area deprivation		Index of multiple deprivation (IMD) score for the local area (lower tier local authority, LTLA) containing the contact's home address. These data were obtained from publicly available national statistics: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019.
	Local area SARS-CoV-2 Incidence		Rolling 7-day average SARS-CoV-2 incidence in the contact's LTLA on the day on the contact's PCR test
	Local area second vaccine uptake		The percentage of those eligible having received two vaccines in the contact's LTLA on the day of the contact's PCR test
	Calendar time		

Table S1. Model covariates.

Category		Example
Disease, problem, or condition under investigation		SARS-CoV-2 infection following contact with an individual known to be infected with SARS-CoV-2
Special considerations related to	Sex and gender	Incidence of SARS-CoV-2 infection is similar in men and women.[8] Men are at increased risk of dying following COVID-19.[9]
	Age	Reported incidence by age has varied during the pandemic, initially limited access to testing resulted in greater reported rates in older individuals who were more likely to be admitted to hospital and tested. However, data from systematic population-based surveys indicate that infections are more common in children and younger adults.[8,10]
	Race or ethnic group	In fortnightly analysis of United Kingdom population survey data, individuals of non-white ethnicities have been intermittently more likely than white individuals to be infected with SARS-CoV-2, after adjustment for other factors including sex, age, geographic region, deprivation and household size and the number of generations living in a household.[8] Individuals of black, south Asian, mixed and other ethnic groups are at increased risk of dying following COVID-19, compared to white individuals, after adjustment including age, sex, obesity, smoking, social deprivation and comorbidities.[9]
	Geography	Throughout the world, reported testing rates, incidence and COVID-19-associated mortality vary. Variation in excess mortality has been used to compare the impact of the pandemic between countries.[11] Excess mortality in the United Kingdom is similar to the United States, with lower excess deaths in several European countries including France and Germany.
Overall representativeness of this trial		This is a national cohort study, based on all community diagnosed index cases with samples processed at 3 national laboratories, i.e., 66.8% of all SARS-CoV-2 index cases in England over the study time period. As such it is expected to be broadly representative of those diagnosed with SARS-CoV-2 in the community. Index cases and their contacts included similar numbers of men and women, but with a small excess of women 52-55% compared to the population of England overall, 51%. The biological sex of cases and contacts was determined from national contact tracing records which allowed entries of "Female", "Male", or "Unknown". No separate records for gender were available. Similarly, case and contact ages (derived from recorded dates of birth) and ethnicity reported by cases and contacts to contact tracing services were used. In keeping with population survey data on SARS-CoV-2 infection,[8,10] cases and their contacts were more likely to be younger adults.

	Administrative data show 85% of the population of England in 2016 were white, 8% Asian, 4% black, 2% mixed and 2% of other ethnicity.[12] Broadly similar proportions of cases and contacts compared to the population of England were of white ethnicity, 79-84%, however cases and contacts studied included relatively more individuals of Asian ethnicity, 9-14%, and relatively fewer of Black ethnicity 2%. The demographic characteristics of contacts who underwent PCR testing (and were therefore included) and those who were not tested (and were excluded) were similar (Table S3).

Table S2. The representativeness of study participants.

		Cases with contacts		Contacts with a PCR test result		Contacts without a PCR test result	
		n	%	n	%	n	%
	Total	374,115	-	173,460	-	487,855	-
Age, years	18-29	122,495	33%	46,489	27%	145,903	30%
	30-39	79,556	21%	34,381	20%	92,342	19%
	40-49	64,199	17%	31,309	18%	82,389	17%
	50-59	63,433	17%	38,754	22%	98,252	20%
	60-69	30,849	8%	16,262	9%	45,581	9%
	≥70	13,583	4%	6,265	4%	23,388	5%
Sex	Female	195,404	52%	95,202	55%	237,898	51%
	Male	177,974	48%	78,143	45%	225,446	49%
	Not recorded	737	-	115	-	24,511	-
Ethnicity	Asian	29,922	9%	10,838	14%	20,115	12%
	Black	7,825	2%	1,855	2%	5,472	3%
	Mixed	7,590	2%	1,670	2%	3,937	2%
	Other	3,579	1%	1,199	2%	2,851	2%
	White	270,815	84%	63,245	79%	126,676	79%
	Not disclosed	3,096	1%	859	1%	2,246	1%
	Not recorded	51,288	-	93,794	-	326,558	-
Vaccine status	Unvaccinated	218,946	59%	73,372	47%	127,051	53%
	Partially vaccinated, ChAdOx1	27,587	7%	13,275	8%	19,447	8%
	Partially vaccinated, BNT162b2	63,807	17%	21,601	14%	34,542	14%
	Vaccinated twice, ChAdOx1	49,060	13%	32,466	21%	40,705	17%
	Vaccinated twice, BNT162b2	14,715	4%	15,747	10%	17,983	8%
	Not recorded	-	-	16,999	-	248,127	-
Variant	Alpha	185,949	50%	-	-	-	-
	Delta	188,166	50%	-	-	-	-

Table S3. Summary of demographic characteristics and vaccination status for index cases and their contacts. Contacts with and without a PCR test performed between 1 and 10 days inclusive following the index case's positive PCR test are shown separately. Column percentages are based on cases or contacts with recorded data, i.e. exclude the rows titled "Not recorded". Missing data for untested contacts reflect that detailed data on contacts was only recorded for many at the point of testing.

Index case vaccination status	n	Age, median	Age, IQR	Female, n	Female, %	Symptomatic, n	Symptomatic, %	Alpha variant, n	Alpha variant, %
Unvaccinated	59,956	35	25 - 50	30,691	51.2	56,184	93.7	43167	59,956
Partially vaccinated, ChAdOx1	8,294	45	40 - 52	4,345	52.4	7,670	92.5	3024	8,294
Partially vaccinated, BNT162b2	20,927	28	22 - 35.5	10,107	48.3	19,634	93.8	3256	20,927
Vaccinated twice, ChAdOx1	15,086	49	36 - 57	7,590	50.3	14,182	94	67	15,086
Vaccinated twice, BNT162b2	4,235	48	32 - 60	2,621	61.9	3,754	88.6	127	4,235

Table S4. Index case demographics, symptom status, and infecting variant by index case vaccine status.

Contact vaccination status	n	Age, median	Age, IQR	Female, n	Female, %	Alpha variant, n	Alpha variant, %
Unvaccinated	65,117	37	26 - 51	34,654	53.2	52,321	80.3
Partially vaccinated, ChAdOx1	12,307	47	41 - 54	7,026	57.1	3,739	30.4
Partially vaccinated, BNT162b2	20,999	30	24 - 37	12,010	57.2	3,829	18.2
Vaccinated twice, ChAdOx1	32,363	53	45 - 58	18,888	58.4	151	0.5
Vaccinated twice, BNT162b2	15,457	51	38 - 60	10,628	68.8	337	2.2

Table S5. Contact demographics, and associated index case variant by contact vaccine status.

Characteristic	PCR tested contacts	PCR-positive contacts	% infected	aRR	95% CI
Variant					
Alpha	60,377	31,326	52	—	—
Delta	85,866	23,341	27	1.24	1.12, 1.38
Index case vaccination status					
Unvaccinated	76,401	35,459	46	—	—
Partially vaccinated, ChAdOx1	11,236	3,878	35	0.90	0.86, 0.94
Partially vaccinated, BNT162b2	31,039	7,947	26	0.88	0.85, 0.91
Vaccinated twice, ChAdOx1	21,421	6,067	28	0.48	0.30, 0.78
Vaccinated twice, BNT162b2	6,146	1,316	21	0.32	0.21, 0.48
Index case vaccination status * Variant					
Partially vaccinated ChAdOx1 * Delta	7,617	2,236	29	1.06	1.00, 1.12
Partially vaccinated BNT162b2 * Delta	27,122	6,162	23	0.94	0.90, 0.99
Vaccinated twice, ChAdOx1 * Delta	21,322	6,053	28	1.58	0.97, 2.56
Vaccinated twice, BNT162b2 * Delta	5,970	1,294	22	1.59	1.07, 2.35
Index case, per doubling of weeks since two weeks after second ChAdOx1 dose				1.08	1.05, 1.11
Index case, per doubling of weeks since two weeks after second BNT162b2 dose				1.13	1.05, 1.21
Index case age	See Figure 2A				
Index case sex					
F	75,678	27,182	36	See Figure 2C	
M	70,565	27,485	39		
Index case symptoms					
Symptomatic	136,534	52,583	39	—	—
Asymptomatic	9,709	2,084	21	0.53	0.50, 0.55
Variant * Index case symptoms					
Delta * Asymptomatic	4,834	779	16	1.12	1.04, 1.22
Event type					
Household or accommodation	97,204	46,437	48	See Figures 2A, 2B	
Household Visitor	16,505	3,284	20		
Events / Activities	16,114	2,560	16		
Work or Education	16,420	2,386	15		
Contact vaccination status					
Unvaccinated	65,117	34,041	52	—	—
Partially vaccinated, ChAdOx1	12,307	3,987	32	0.94	0.91, 0.98
Partially vaccinated, BNT162b2	20,999	6,756	32	0.85	0.82, 0.88
Vaccinated twice, ChAdOx1	32,363	7,241	22	0.40	0.27, 0.59
Vaccinated twice, BNT162b2	15,457	2,642	17	0.15	0.11, 0.21
Contact vaccination status * Variant					
Partially vaccinated ChAdOx1 * Delta	8,568	2,299	27	0.73	0.69, 0.77
Partially vaccinated BNT162b2 * Delta	17,170	5,040	29	0.79	0.76, 0.83
Vaccinated twice, ChAdOx1 * Delta	32,212	7,221	22	1.04	0.70, 1.53
Vaccinated twice, BNT162b2 * Delta	15,120	2,611	17	1.28	0.92, 1.78
Contact, per doubling of weeks since two weeks after second ChAdOx1 dose				1.13	1.10, 1.16
Contact, per doubling of weeks since two weeks after second BNT162b2 dose				1.27	1.21, 1.34
Contact age	See Figure 2B				

Characteristic	PCR tested contacts	PCR-positive contacts	% infected	aRR	95% CI
Contact sex					
F	83,206	30,047	36	See Figures 2C, 2D and S2	
M	63,037	24,620	39		
Index of multiple deprivation, per 1000 change, higher indicates more deprived				1.01	1.01, 1.01
Local SARS-CoV-2 incidence	See Figure S3				
Study day	See Figure S4				
Event type * Contact sex	See Figure S2				
Index case sex * Contact age	See Figure 2D				
Index case sex * Contact sex	See Figure 2C				
Event type * Index case age	See Figure 2A				
Event type * Contact age	See Figure 2B				
Index case age * Contact age	See Figure 2E				

Table S6. Multivariable logistic regression analysis of associations of PCR-positive results in contacts. aRR, adjusted rate ratio; CI, confidence interval; Main effects are shown and * indicates an interaction term. For index case and contact vaccination status interactions with lineage, combined effects are shown in Table 1. Non-linear relationships and associated interactions are shown in Figures 2 and S2-S4 as indicated. There is an interaction between variant and contact age, such that all rate ratios for variant are shown at a contact age of 18 years.

	Alpha		Delta		Delta vs. Alpha	
Characteristic	aOR	95% CI	aOR	95% CI	Interaction OR	95% CI
Impact on onward transmission: Case vaccination status						
Unvaccinated	—	—	—	—	—	—
Partially vaccinated, ChAdOx1	0.89	0.85, 0.94	0.95	0.91, 1.00	1.07	1.00, 1.14
Partially vaccinated, BNT162b2	0.88	0.84, 0.92	0.84	0.81, 0.87	0.96	0.91, 1.01
Vaccinated twice, ChAdOx1	0.48	0.25, 0.93	0.78	0.71, 0.85	1.60	0.83, 3.07
Vaccinated twice, BNT162b2	0.30	0.18, 0.49	0.48	0.35, 0.66	1.62	1.03, 2.58
Contact vaccination status						
Unvaccinated	—	—	—	—	—	—
Partially vaccinated, ChAdOx1	0.98	0.94, 1.03	0.73	0.70, 0.77	0.75	0.70, 0.80
Partially vaccinated, BNT162b2	0.89	0.86, 0.93	0.70	0.68, 0.73	0.79	0.75, 0.83
Vaccinated twice, ChAdOx1	0.45	0.29, 0.69	0.46	0.42, 0.50	1.02	0.66, 1.56
Vaccinated twice, BNT162b2	0.15	0.09, 0.22	0.21	0.17, 0.27	1.51	0.98, 2.34

Table S7. Sensitivity analysis: Relationship between PCR-positive results in contacts, and index case and contact vaccination status according to Alpha/Delta variant in the index case (restricting to contacts tested 2 to 7 days inclusive after an index case). Results for those with two vaccine doses are estimated at day 14 post second vaccine, see Figure S7 for trends with time post-second vaccine. aRR, adjusted rate ratio, CI confidence interval. Adjustment made for contact event type; index case factors - age, sex, and symptom status; contact factors - age, sex; local deprivation, local SARS-CoV-2 incidence and calendar time.

	Alpha		Delta	
	Increase in Ct value vs. unvaccinated	95% CI	Increase in Ct value vs. unvaccinated	95% CI
Two doses of BNT162b, 2 weeks after second dose	4.87	2.06-7.68	3.86	2.88-4.83
Two doses of BNT162b, 12 weeks after second dose	6.58	4.82-8.35	1.41	1.19-1.64
Two doses of ChAdOx1, 2 weeks after second dose	4.43	0.51-8.35	0.60	0.30-0.90
Two doses of ChAdOx1, 12 weeks after second dose	5.41	1.23-9.59	0.45	0.25-0.64

Table S8. Changes in index case Ct values at diagnosis associated with vaccination.
Estimates show the increase in Ct value seen in index cases at diagnosis compared with an unvaccinated index case. Separate estimates are shown by vaccine type and time since second vaccination for Alpha and Delta variant infections. Linear regression estimates were adjusted for vaccine, variant, time since second vaccination, index case age, symptoms, and sex, and calendar time. There was no evidence of an effect of time since second vaccination for Alpha infections following BNT162b (coefficient per doubling of time since two weeks post second vaccination=0.50 [95%CI -0.64,1.63]) or ChAdOx1 (0.28 [-1.86,2.42]) or for Delta infections following ChAdOx1 (-0.05 [-0.15, 0.07]). However, for Delta infections following BNT162b, increases in Ct value vs. infections in unvaccinated index cases were smaller as time since second vaccination increased (-0.71 [-0.98, -0.43]). CI, confidence interval.

Index case vaccine status	Variant	Total effect (95% CI)	Average mediation effect, via Ct value (95% CI)	Average direct effect, not via Ct value (95% CI)	Proportion mediated (95% CI)
Vaccinated twice, BNT162b2	Alpha	-0.37 (-0.48, -0.15)	-0.07 (-0.12, -0.04)	-0.30 (-0.43, -0.04)	0.18 (0.09, 0.64)
Vaccinated twice, BNT162b2	Delta	-0.17 (-0.21, -0.13)	-0.04 (-0.05, -0.03)	-0.13 (-0.18, -0.08)	0.23 (0.17, 0.33)
Vaccinated twice, ChAdOx1	Alpha	-0.37 (-0.50, -0.03)	-0.07 (-0.12, -0.02)	-0.30 (-0.45, 0.07)	0.16 (0.01, 0.80)
Vaccinated twice, ChAdOx1	Delta	-0.10 (-0.12, -0.08)	-0.01 (-0.01, 0.00)	-0.09 (-0.11, -0.07)	0.07 (0.05, 0.10)
Partially vaccinated, BNT162b2	Alpha	-0.06 (-0.08, -0.04)	-0.02 (-0.03, -0.02)	-0.04 (-0.05, -0.02)	0.39 (0.30, 0.53)
Partially vaccinated, BNT162b2	Delta	-0.06 (-0.06, -0.05)	-0.01 (-0.01, -0.01)	-0.05 (-0.06, -0.04)	0.14 (0.11, 0.17)
Partially vaccinated, ChAdOx1	Alpha	-0.05 (-0.07, -0.03)	-0.02 (-0.02, -0.01)	-0.03 (-0.05, -0.02)	0.33 (0.23, 0.53)
Partially vaccinated, ChAdOx1	Delta	-0.04 (-0.05, -0.03)	0.00 (-0.01, 0.00)	-0.03 (-0.05, -0.02)	0.12 (0.07, 0.19)

Table S9. Extent of vaccine-associated reductions in transmission mediated via index case Ct values at diagnosis. The reference group for each comparison is unvaccinated index cases. Effects reported are averaged over the dataset, i.e. both vaccinated and unvaccinated contacts and all times since second vaccination in index cases. Because times since second vaccination to infection were typically longer for BNT162b2 than ChAdOx1, the average total effect for BNT162b is more similar to ChAdOx1 than is seen in Figure 1 where a representative range of times since second vaccination are shown. See Table S8 for details of the effect of vaccination on Ct values by vaccine type and variant. CI, confidence interval.

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